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CITIZEN PETITION 00P-1607/CP 1

November 7, 2000

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Dockets Management Branch

Food and Drug Administration

Department of Health and Human Services, rm 1-23

Rockville, MD 20857

The undersigned submits this petition to request the Commissioner of Food and Drugs, revoke the implantation of silicone gel-filled breast implants (SGFBIs) for any reason, in light of new research documenting the significant release of platinum in a reactive valence from intact implants. FDA's own research "Prevalence of Rupture of Silicone Gel Breast Implants Revealed on MR Imaging in a Population of Women in Birmingham, Alabama (October 2000) documents 77% or 265 of 344, had at least one breast implant that was rated as ruptured or indeterminate. Silicone gel was found outside the scar capsule in 73 women or 21.2% of implanted women in this study. It would be presumed that toxic hypersensitizing platinum would also leak outside the scar capsule. Thus, making the risks of chronic exposure to toxic platinum outweigh the benefits of this class III device which, by law, must be proven safe and effective. As no manufacturer of SGFBIs has in the thirty year history of their use, been able to prove them to either be safe or effective and since other forms of breast reconstruction are available, no justification can be envisioned to allow the continued marketing of this defective toxic device.

Upon confirmation from other independent research, the undersigned also requests the Commissioner of Food and Drugs issue a public health alert as to breast-feeding or pregnancy to avoid possible genotoxic effects and advice as to removal to avoid potential or worsening health consequences. It is further requested that all remaining inventories of SGFBIs in the United States be destroyed in order to protect the health of women and our future generations.

In support of the above requests, I submit the following:

1. Published peer-reviewed research "Release of Low Molecular

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Weight Silicones and Platinum from Silicone Breast Implants" (1997) by Baylor College of Medicine documents the ability of new equipment (GC-AED, GC/MS, ICP-MS) to detect silicones in the nanogram range and platinum in the parts per trillion range. This research also studies the rates at which low molecular (LM) silicones and platinum leak through the intact implant outer shell into surrounding media under a variety of conditions. Leakage was greatest when the surrounding medium was lipid-rich and, potentially, could lead to significant accumulation within lipid rich tissues (breast tissue, brain tissue, myelin, etc.). Previous research "Measurement of Platinum in Biomedical Silicones by ICP-MS" (1995) and subsequent research "Platinum Concentration in Urban Road Dust and Soil, and in Blood and Urine in the United Kingdom" (1998), both used ICP-MS to measure platinum release from either silicone gel-filled implants or concentration in body fluids. The 1995 research by El-Jammal and Templeton found platinum was present at approximately 4.5 micrograms per gram (-1) in a silicone breast implant but was absent from medical grade silicone oil, indicating that platinum used as a catalyst in polymerization was not removed from implanted devices.

2. New research soon to be submitted for publication by Ernest Lykissa, Ph.D., using ICP-MS to measure the amount of platinum release and ion chromatography to speciate the platinum release, has shown that of the eight SGFBIs tested, all eight had significant release of platinum. Most of which was in a toxic hypersensitizing reactive valence (see attached table - Attachment 1). See included symptoms and diagnoses of the explanted women in this study (Attachment 2 - further documentation will be provided upon request). While this is not a large study, a small study by Semple et al., "Breast Milk Contamination and Silicone Implants" (1998) of fifteen lactatin g women with breast implants measuring silicon (the second most abundant element on earth) is quoted in the FDA's Breast Implants - An Information Update 2000. Furthermore, the FDA and the Institute of Medicine (IOM) uses this small study to erroneously imply that breast-feeding by breast implanted women is safe.

3. The manufacturers of implants agree that "platinum salts" (chloroplatinic acid) can cause systemic disease in humans as a result of toxic and/or hypersensitivity reactions. The manufacturers claim there are no "platinum slats" in silicone gels and elastomers. Court stamped documents indicate the platinum catalyst used by the manufacturers is hexachloroplatinic acid or chloroplatinic acid

(platinum salts). The manufacturers, in private correspondence to the IOM, claim any platinum residual left in SGFBIs is in a zero oxidate state or is colloidal, elemental platinum. The manufacturers' internal documents, the testimony of manufacturers' employees, and the admissions of the manufacturers in the Supplemental Submission on Platinum all point to the conclusion this is not true. In document DCCKK A028229 Dow Corning Corporation Proprietary Information for mammary implant material formulation Q7-2046, it lists chloroplatinic acid among the ingredients. A foot note at the bottom states "(a) denotes ingredient removed during manufacturing process". There is no (a) after chloroplatinic acid.

4. Roger L. Wabeke, MSc, MscChE, CHMM, PE, President of Chemical Risk Management estimates the amounts of platinum salts present in two 260 cc silicone gel implants demonstrate an in vivo platinum salts exposure to platinum in women with silicone gel implants 1000 times greater then the occupationally allowed limit. The OSHA permissible air-borne exposure limit is 0.002 mg Pt/m3 for soluble platinum salts in industrial workers (OSHA 1981). Dr. Wabeke states "How much ionized platinum remains in vivo is debatable, but any analytically-detectable amount, in my view, given the high toxicity and biological reactivity of soluble ionized platinum, is too much". Wabeke sites the research by Agnew et al., "Neuropathological Effects of Intracerebral Platinum Salt Injections" which studied the effects of multiple injections of two platinum salts (potassium chloroplatinate and chloroplatinic acid) on cat brain. He concludes the amounts of platinum used in this research are within the same order of magnitude as those detected in the silicone implants. Furthermore, Schuppe et al., "T-Cell-Dependent Popital Lymph Node Reactions to Platinum Compounds in Mice" (1992) demonstrated immunogenicity after injections of hexachloroplatinate in mice. As in the Agnew et al research, the amounts of platinum used are in the same range as amounts of platinum in the silicone implant materials. Wabeke states "Clearly, breast implants weigh more than one gram, so the amount of implanted platinum in humans exceeds treated-mice amounts."

5. The research of Potter, et al., "Induction of Plasmacytomas with Silicone Gel in Genetically Susceptible Strains of Mice" (1994) establishes that platinic chloride is a water-soluble form of the metal that is used as the preferred catalyst in medical silicone gels and elastomers. Their work further establishes that any soluble platinum leaching from an implant would be expected to distribute in the circulation as a chloroplatinate. Dow Corning research on nipples for

baby bottles determined that platinum leached out into a water solution as well as the other solutions used including ethanol in water, acatic acid and olive oil.

6. The toxicity and hypersensitivity of platinum salts is already known and well documented. The following statements can be found in the book "Platinum" published by the World Health Organization and the International Programme on Chemical Safety (1991): "During the course of a reproduction study, behavioral effects were observed in the offspring of mice treated with sodium hexachloroplatinate... The symptoms typical of platinum salt sensitization (Brooks 1990) include watering of the eyes, sneezing, tightness of the chest, wheezing, breathlessness, coughing, eczematous and urticarial skin lesions, and signs of mucous membrane inflammation...The compounds mainly responsible for platinum sensitizations include hexachloroplatinic acid...The symptoms usually worsen with increasing duration of exposure but generally disappear when the subject is removed from exposure. However, Schultze-Werninghaus, et al., (1989) reported that after long duration exposure following sensitization, individuals may never become completely free of symptoms...Only limited experimental data are available for platinum effects on reproduction, embryotoxicity, and teratogencity...Several platinum compounds have been found to be mutagenic in a number of bacterial systems."

7. Further documentation of toxicity and hypersensitivity of platinum can be found in the book "Toxicology and Biological Monitoring of Metals in Humans" (1986). "After inhalation of platinum metal, lung clearance is rather slow, and kidney and bone accumulate platinum...There is some transplacental platinum passage...In an extensive survey of California autopsy tissues, only 4.7% contained detectable platinum (Stokinger 1981). After subcutaneous fat; kidney, pancreas, and liver had the highest detection frequencies...After ingesting drinking water containing platinum for 8 and 9 days, highest concentrations were in kidney and liver (Holbrook 1975)...Simple (platinum) salts cause vomiting and diarrhea with bloody stools...Platinum complexes cause epileptiform convulsions, coma, and death.. Non-lethal doses cause hyperirritability, restlessness, motor excitement, and delayed heart action (Stokinger 1981)...In rats, signs of acute oral toxicity also include dystrophic changes in the liver and kidneys (Veselov 1977)...Platinum compounds bind to DNA molecules (NAS 1977)...A platinum complex has been reported to interfere with mitocrondrial transport of calcium (Stokinger 1981)...An asthma-like syndrome

called platinosis occurs after preliminary eye and upper respiratory tract irritation with cough, tightness of the chest, wheezing, and shortness of breath. The severest cases experience cyanosis, diaphoresis, feeble pulse, and clammy coldness of the extremities (Browning 1969)...Scaling, dryness, cracking, and eczematous patches characterize the dermatitis (Browning 1969)...The platinum diammine slats are immunosuppressive (Stokinger 1981). A low-grade fibrosis has been described in the lungs of some workers with platinosis (Browning 1969)...no information on teratogenicity".

8. Research by Kala, et al., "Low Molecular Weight Silicones are Widely Distributed after a Single Subcutaneous Injection in Mice" (1998) indicates highest levels at 3, 6, or 9 weeks were found in the mesenteric lymph nodes, ovaries, and uterus, but all organs examined contained cyclosiloxanes. At one year, highest levels were found in the mesenteric lymph nodes, abdominal fat, and ovaries. Animals receiving linear siloxanes were found to have manimum levels in the brain, lungs, and mesenteric lymph nodes at 9, 12, and 15 weeks. Detectable levels are found to persist for at least a year, which is approximately 40% of the life span of a mouse. Whether these compounds persist indefinitely and to what extent is an important area for additional study. The wide spread distribution of low molecular weight silicone and their persistence raises the issue of possible untoward consequences.

9. In a public statement made 12/1/98, Michael W. Lieberman, MD, Ph.D., Department of Pathology, Baylor College of Medicine stated "I believe there is significant evidence that components of breast implants are highly toxic and may cause serious health effects." Research (Lieberman et al, 1999) published in the DHHS sponsored Environmental Health Perspectives clearly shows that cyclosiloxane-platinum silane (distilate) is toxically equivalent to toxins like carbon tetrachloride (equivalent median lethal dose LD50).

10. Based on the Agnew research (1975) suggesting an inhibitory effect of platinum on brain enzymes, Michael Harbut, MD, MPH (March 1999 Plaintiffs Submission) concludes that platinum salts can cause brain disease. Ernest Lykissa, Ph.D. (March 1999 Plaintiffs Submission) states "the evidence clearly demonstrates the propensity of the cyclosiloxane-platinum silane mixture, to accumulate in the brain tissue of living animals and to persist there for the duration of one year following a signal administration. It is highly unlikely, that the rich in lipids brain tissues, that depend to a great extent on lipophilicity (lipid solubility) for the transmission of electric, in

nature, nerve impulses are not affected by high concentrations of very lipid soluble cyclosiloxane-platinum silane toxins, residing on the membranes of their constituent cells."

11. The toxic and hypersensitivity reactions to platinum salts can range from asthma,rhinorrhea, tinnitus, conjunctivitis, urticaria, fatigue syndromes secondary to impaired oxygen exchange, neurotoxicity, sicca syndrome, and macular rashes. Research that document these conditions in women with breast implants or their children born after implantation when examined by treating physicians, include the following:

(a) Brawer AE "Chronology of Systemic Disease Development in 300 Symptomatic Recipients of Silicone Gel-filled Breast Implants" J. Clean Technol Environ Toxicol & Occup Med, 1996, 5; (3): 223-233

(b) Harbut MR, et al "Asthma in Patients with Silicone Breast Implants: Report of a Case Series and Identification of Hexachloroplatinate Contaminant as a Possible Etiologic Agent" Israel J of Occup Health 1999, 3 (1) 73-81

(c) Levine JJ, et al "Esophageal Dysmotility in Children Breast-fed by Mothers with Silicone Breast Implants" Digestive Diseases and Sciences, 1996, 41; (8): 1600-1603

(d) Ericsson AD "Syndromes Associated with Silicone Breast Implants: A Clinical Study and Review" J of Nutritional & Environ Med 1998, 8: 35-51

(e) Bridges AJ, et al "A Clinical and Immunologic Evaluation of Women with SBI and Symptoms of Rheumatic Disease" Annals of Internal Medicine, June 1993, 18; (12) 926-936

12. An immunosuppressive reaction to platinum salts is documented in the following research:

(a) Campbell AW, et al "Suppressed Natural Killer Cell Activity in Patients with Silicone Implants: Reversal Upon Explantation" Toxicology and Industrial Health, 1994; 10, (3) 149-154

(b) The IOM report states "Consistent with animal toxicology studies noted earlier, it appears that NK cells in humans might be affected by exposure to silicone gel, since removal of silicone breast implants was followed by an increase in NK-cell function in 50% of women

studied by Campbell. This research is supported by the, as yet, unpublished data (see Sttachment 3) submitted by Patricia D. Salvato, MD (Sept. 2000) "Silicone Breast Implants and Natural Killer Cell Numbers". Of 633 breast implanted patients evaluated by Dr. Salvato, the range of natural killer cell counts was from 8 to 256, with an average of 110. Of 136 healthy controls, the range was from 320 to 550, with an average of 410. Dr. Salvato states "From this data it can be postulated that silicone has a direct and toxic effect on natural killer cell numbers in patients with silicone breast disease. It has been reported in the medical literature that natural killer cell activity may somehow impinge on the central nervous system. Natural killer cells are capable of crossing the blood brain barrier and are present in the brain and certain pathological states. It has also been reported that natural killer cells express receptors for neuropeptides and hormones. It has also been shown that products of activated natural killer cells are damaging to the neurons. Some of the activated natural killer cells infiltrating normal systems of patients, thus manifesting as a cause of neuro-endocrine abnormalitites. This research lend more evidence to the growing medical literature supportive of silicone's toxic effects on the immune system, central nervous system, and peripheral nervous system."

13. The argument could be made that there are no published controlled epidemiological studies demonstrating a risk of allergy (hypersensitivity) related to breast implants, only because no study has actually examined and tested breast implanted patients. Compelling new research by Brawer (2000) demonstrating improvement of systemic phenomena and disease amelioration following explantation, provides supportive evidence for the existence of a novel illness triggered by silicone gel-filled devices. The argument that a large controlled epidemiological study documenting a health risk to platinum salts is needed before gel-filled breast implants can be removed from the market is not applicable here because of the enormous potency of platinum salts. To quote Drs. Niezborala and Garner in regard to industrial contact "At no stage should a worker be able to come into contact with a solution or a solid containing these particular complex platinum salts". In other words, there is no "safe" level of platinum salts in implanted devices. Furthermore, platinum salts are considered so toxic that the consensus opinion in Occupational Medicine is that platinum allergy exists in a worker presenting with classic allergy symptoms (who is exposed to platinum salts) until proven otherwise according to Machael Harbut, MD.

From 1985 until January 2000, FDA has received 127,770 adverse reaction reports for SGFBIs (adverse events include death, life-threatening injury or illness, hospitalization, disability, birth abnormality, or medical intervention to prevent permanent impairment or damage). To allow this toxic defective class III device to remain on the market is egregious conduct on the part of the manufacturers, who are required by law to prove breast implants to be safe, and the FDA, whose mission is to protect the consumer and their unborn children. The Nuremberg Code states a person should give consent and exercise free power of choice without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior from of constraint or coercion. They also should have sufficient knowledge and comprehension of the elements of the subject matter involved to make an understanding and enlightened decision. Furthermore during the course of the experiment, the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill, and careful judgment required of him, that a continuation of the experiment is likely to result in injury, disability or death to the experimental subject. While women can remove their implants, there is no way for them to end the experiment and remove the platinum-cyclosiloxane complexes when it spreads to all parts of their bodies. Safety must matter.

ENVIRONMENTAL IMPACT -

I request a waiver on the environmental assessment under Sec. 25.31. I believe there will be a positive environmental impact when SGFBIs are removed from the market because there will be less toxic waste to dispose of when implants are removed. I believe women and their children will experience less toxic poisoning and environmental injury when SGFBIs are no longer placed in their bodies or when silicone, silica, or its components (toxic and hypersensitizing platinum) are passed in the placenta or in breast milk.

ECONOMIC IMPACT -

Revoking the implantation of SGFBIs will help balance the budget and reduce the deficit. Less money will have to be paid out when former hard working productive women implanted with SGFBIs become disabled, can no longer work, lose their insurance, or can no longer care for themselves and their families (refer to the U.S. Justice Dept. claim in the Dow Bankruptcy). This should have a favorable

economic impact on the individual considering SGFBIs in long term health care savings. Just because there is insufficient data does not mean that a new disease as a result of exposure to toxic and hypersensitizing chemicals does not exist, it simply means that the long-term studies have not been done. We do not know the frequency of complication or the severity of disease, because a national registry was never mandated. Because of the latency period of systemic symptoms to appear, doctors and women have been slow to recognize their disease and that of their children born after implantation, may be related to their implants. The FDA's Scleroderma Court Study and the NCI's Study of 13,500 Breast Implanted Women should soon document that something has gone tragically wrong. Furthermore the FDA's own research as published in the Annual Report 1998 Office of Science and Technology documents statistically significant elevated autoantibodies to collagen type I, collagen type II and anti-DNA were detected in serum of patients with Connective Tissue Disease (CTD), CTD + silicone implants, and silicone implants without CTD.

A possible negative impact to the economy might be a loss of income for the plastic surgeons who have come to depend on the easy money generated by breast implants, the repeat surgeries they require, and the high cost of explantation when rupture or severe gel bleed occur. However, with the availability of saline-filled implants and other reconstruction options, this should not be an undue hardship. When choice may damage a woman's health and that of her unborn children, they must be protected.

Marlene Keeling, President

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(2) Lykissa ED, Kala SV, Hurley JB, Lebovitz RM "Release of Low Molecular Weight Silicones and Platinum from Silicone Breast Implants" Analytical Chemistry, Vol. 69, No. 23, December 1, 1997

(3) El-Jammal A, Templeton DM "Measurement of Platinum in Biomedical Silicones by ICP-MS" Analytical Proceedings including Analytical Communications, August 1995, Vol. 32

(4) Farrago ME, et al "Platinum Concentrations in Urban Road Dust and Soil, and in Blood and Urine in the United Kingdom" Analyst, 1998 Mar; 123, 451-454

(5) Semple JL, et al "Breast Milk Contamination and Silicone Implants: Preliminary Results Using Silicon as a Proxy Measurement for Silicone" Plast Reconstr Surg 1998 Aug; 102, (2): 528-33

(6) Schuppe HC, et al "T-Cell-Dependent Popliteal Lymph Node Reactions to Platinum Compounds in Mice" Int Arch Allergy Immunol 1992; 97: 308-314

(7) Plaintiffs' Supplemental Submission on the Chemistry and Toxicology of Platinum. Master File CV 92-P-10000-S, March 25, 1999

(8) Safety of Silicone Breast Implants. IOM, July 1999, p. 50,51,81,82
(9) DCCKK A028218-19, A028224-25, A0228229-30-33-34-35-36

(10) Agnew WF, et al "Neuropathological Effects of Intracerebral Platinum Salt Injections" Surg Neurol, 1075, 4: 438-448

(11) Potter M, et al "Induction of Plasmacytomas with Silicone Gel in Genetically Susceptible Strains of Mice" J of the NCI, 1994 Jul 20; 85,

(14): 1058-1065

(12) Kala SV, et al "Low Molecular Weight Silicones Are Widely Distributed after a Single Subcutaneous Injection in Mice" Am J of Pathol, March 1998, 152, (3): 645-649

(13) Brawer AE "Amelioration of Systemic Disease after Removal of

Silicone Gel-filled Breast Implants" J of Nutritional & Environ Medicine 2000: 10, 125-132

(14) Lieberman MW, et al "Cyclosiloxanes Produce Fatal Liver and Lung Damage in Mice" Environmental Health Perspectives, February 1999: 107, (2); 161-165

PETITION

ACTION REQUESTED: That the United States Food and Drug Administration issue a warning statement, or cause appropriate parties to issue warning statements, consistent with the known, available science in regard to the safety of medical devices manufactured with silicone which has been catalyzed with hexachloroplatinate.

This warning statement should include at a minimum the following statements (or words to this effect):

(1) In the workplace setting, the medical literature states that no person should come into contact with a liquid or solid containing the chemical catalyst called hexachloroplatinate. Some products sold for human internal and external use contain this catalyst, including silicone gel breast implants, silicone-envelope saline-filled breast implants, certain implanted fluid shunting devices, other implanted devices used in plastic and bone surgery and dermatological-use silicone gel used to help reduce scarring.

(2) Although no large scale human epidemiological studies in regard to platinum-caused disease caused via medical devices have been undertaken, in the workplace setting,

persons with evidence of asthma and rhinitis who have been exposed to hexachloroplatinate are considered to have a disease caused by hexachloroplatinate until proven otherwise.

(3) Extremely small amounts of hexachloroplatinate are known to trigger immunologic reactions, cause asthma and damage brain cells, in addition to the other health effects which have been reported in the medical literature.

(4) Although there has been disagreement over the exact type of platinum emitted by silicone gel breast implants, there is no disagreement that hexachloriplatinate is used in their manufacture. Furthermore, there has been no disagreement that even intact breast implants emit some form of platinum.

STATEMENT OF GROUNDS: Attached to this Petition is a document prepared for the United States Federal Court which had contemplated the legal issues invoked by illnesses perceived to be caused by silicone gel breast implants. It sets forth the scientific grounds for the Petitioner's request. It does not include the recently presented work of E. Lykissa, PhD. in which Dr.Lykissa speciated platinum ions liberated from Silicone Gel Breast Implants, providing a basis for even a stronger warning than this Petition requests.

This Attachment was prepared after the Petitioner acting individually notified Judge Pointer of serious factual errors published by his so-called Science Panel in regard to the biological activity of platinum catalyst. Although the Petitioner is unaware of the entire spectrum of ensuing legalities, the Attachment was ultimately prepared for the benefit of the so-called Science Panel at Judge Pointer's initiation.

Based on a review of the published depositions of the so-called Science Panel, it is clear that this document was not read in its totality by the so-called Science Panel.

Furthermore, this document was not contemplated by the National Academy of Science Committee assembled in regard to the issue of Silicone Gel Breast Implants. It was completed after the close of it's deliberations.

CERTIFICATION: The Attachment includes in it the criticisms raised by the attorneys defending the manufacturers of Silicone Gel Breast Implants, and the science which answers them, providing a concrete grounding for granting of this petition. It is the Petitioner's understanding that a separate document exists which was assembled by these defense attorneys.

The Petitioner does not possess a copy of this document. Although it is the Petitioner's belief that criticisms raised were answered in the Attachment, it is furthermore the Petitioner's belief that it would be much easier for the FDA to get a copy of this document than it is for the Petitioner.

Submitted October 16, 2000.

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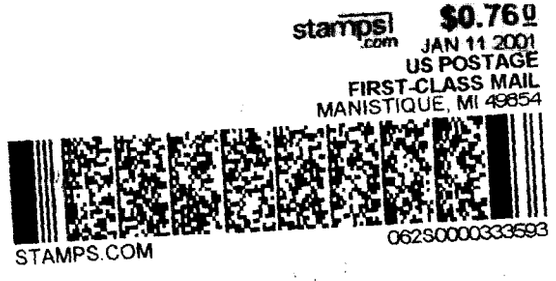

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